Cognition, Attention and Anxiety: Implications for Everyday Functioning for individuals with VCFS/22q11.2 Deletion Syndrome

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Inaugural VCFS Educational Foundation Webinar
September 20, 2011

Intro/Overview

Cognitive Impairments
- several interacting areas of dysfunction

Arousal, Stress and Anxiety
- coping modulates cognitive/academic/behavioral function
- risk/protection for psychiatric outcomes?

Thoughts about developmental impact on wider outcomes

Assessments in the MIND 22q11.2DS Clinic
- Neuropsychology, Developmental/Behavioral Pediatrics, Psychiatry

Case Studies & Evidence Based intervention strategies

Interactive Discussion & Questions
Neuropsych/Cognitive Profile

Standardized tests show a stable pattern for 22q11.2DS population

- Full Scale IQ: 70-85 (±15)
- Verbal Domains (VCI) > Nonverbal (PRI) (in most children)
- Receptive > Expressive language
- Rote memory strong, complex memory verbal and all spatial memory is poor. Working memory is poor
- Reading/Spelling are relative strengths, but comprehension poor
  - “learning to read” goes OK but “reading to learn” is very challenging!
- Attention (selective and “executive”) is impaired

Experimental studies show: visuospatial, temporal, numerical issues

How challenging is life @ 10yrs old when functioning like 7.5yrs old?
- how do all the factors involved interact to affect outcomes?

Objects, Space & Numbers

Space and Time are very abstract concepts that have “scale” but no actual values attached to them

- we use mental “units” to break them up meaningfully
- have to learn “how” much is a(n): inch/second, foot, hour
- numbers were invented to describe “how many” units

What if your “mental units” don’t match parts of the real world accurately?

- space/time estimates will be wrong, numbers won’t make sense
- “digital camera” analogy of mental representation -> Crowding

This explanation guides the design for novel interventions

- Grant under review @ NIH, game prototype now exists!
“Crowding” & Attentional Resolution

Spatial Resolution & Comparison

Tests ability to mentally represent & compare quantitative information
Tests specificity/generality impairment
- spatial magnitudes & auditory pitch

Task uses limited adaptive algorithm
“Target” initially 50% of length of “standard”
- if 3/4 trials correct, reduce difference 50%
- else increase difference by 50%
- all stimuli followed by mask
Q: First or second blue bar longer?

Auditory pitch task tests specificity

From Cavanagh, 2004
Spatial Resolution & Comparison

Adaptive task indicates reduced resolution of analog spatial but not auditory pitch representations.

Temporal Resolution

Tests resolution of temporal attention.

“Oddball” alien flickers out of phase with other 3. Pick the oddball at different flickering speeds. At what speed, i.e. temporal resolution does detection performance drop?

All groups well above 25% chance. All best at 2-4 cycles/sec. 22q11.2DS group 25% worse.
Cognitive Control

Go/No-Go Response Inhibition Task:

- “Go” trials (75%): press a button as quickly as possible to “whack” the mole (in its various disguises!)
- “No-Go” trials (25%): do NOT press button to avoid “squashing” the vegetable

Cognitive Control - Overall Results

Unlike TD children, most children with 22q11.2DS do not do better when more “Go” trials indicate an upcoming “NoGo” trial
Attention, Arousal & Behavior

Attention functions to select among competing, salient inputs
- Salience changes dynamically and is driven internally & externally
  - External:
    - What teacher is writing on the board
    - What the kid next to me is doing
  - Internal:
    - How much do I want/need to understand this math?
    - How much does math make make head/tummy hurt?
    - How much yummier does that cookie look when dieting?

Stress & Anxiety alter arousal & arousal alters salience
- Threshold for what enters consciousness drops (survival)
- Suddenly more things are competing for (impaired) attention
- “Spotlight of attention” is pulled in multiple directions
- Nothing is attended long/deeply enough for learning e.g. math

Might this explain significant proportion of ADHD Dx?

Biological Indicators of Stress

Mock MRI scanner used to measure stress hormone (Cortisol) levels to mild stressor

Average salivary Cortisol levels before mock-MRI practice session (Time 1), 25 mins AFTER Time 1 (i.e. Time 2) and TOTAL Cortisol output.

Total and Time 2 Cortisol levels significantly higher in children with 22q11.2DS

Time 1 levels trend towards statistical significance. Beaton et al. unpublished
Anxiety & Functional Abilities

Adaptive function: how well you complete age appropriate tasks

Adaptive function is NOT related to overall IQ In our 22q sample!

Adaptive function IS related to anxiety levels

Angkustsiri et al., in preparation

Arousal, Anxiety & Inattention

Michelle Y Deng, Ph.D.
Small study, but shows impact of anxiety, perhaps on psychosis

Psychotic Symptoms Common by Adolescence

<table>
<thead>
<tr>
<th>Study</th>
<th>Measure</th>
<th>N</th>
<th>Age (yrs)</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feinstein et al., 2002</td>
<td>DICA-P, KSADS-PL</td>
<td>28</td>
<td>12.3 ± 3.9</td>
<td>4 with delusions or hallucinations.</td>
</tr>
<tr>
<td>Baker &amp; Skuse, 2005</td>
<td>CAPA</td>
<td>25</td>
<td>16 ± 2</td>
<td>21 vs 3 controls had at least one schyzotypal symptom, unspecified.</td>
</tr>
<tr>
<td>Debanné et al., 2006</td>
<td>DICA-P, KSADS-PL</td>
<td>43</td>
<td>10.6 ± 11.2</td>
<td>12 with positive symptoms, auditory hallucinations specified for 5 preadolescents.</td>
</tr>
<tr>
<td>Vorstman et al., 2007</td>
<td>KSADS-PL</td>
<td>60</td>
<td>13.4 ± 2.7</td>
<td>16 with hallucinations, delusions, or paranoia.</td>
</tr>
</tbody>
</table>
Psychiatric Risk and Protection

Joel Stoddard, M.D.

Cannon et al. Schizophr Bull. 33:3 2008

Summary

Now able to integrate many research areas for translation/intervention

- mind/brain changes underlying cognitive impairments
- allostatic load of challenges & neurobiological stress/anxiety response modulate coping success (+/- family/community supports)
- cognitive control changes & common schizophrenia-related symptoms in adolescence may be risk/protection factors
- medical history & other subtyping explorations may identify further ideas about potential outcomes

ALL of these will be affected by background genes, experience etc

but combined basic & clinical research are starting to indicate ways to explain, treat and perhaps alter outcomes
Thanks

**MOST important**: Kids who participated & their families!!

Majority of the work presented here was done by:

- Margie Cabaral, Freddy Bassal, Heather Shapiro, Ling Wong, Elliott Beaton Ph.D., Siddarth Srivastava Ph.D., Michelle Deng Ph.D., Joel Stoddard, M.D., Danielle Harvey, Ph.D., Kathy Angkustsiri M.D., Nicole Tartaglia M.D., Ingrid Leckliter Ph.D., Janice Enriquez Ph.D.

With important contributions from:

- Tracy Riggins Ph.D., Yukari Takarae Ph.D., Mendoza M.A., Leeza Kondos & others

- UC Davis Center of Excellence in Developmental Disabilities